Local-clonal expansion of infiltrating T lymphocytes in chronic encephalitis of Rasmussen.

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Rasmussen's syndrome is a progressive and intractable form of epilepsy characterized pathologically by focal brain inflammation with large numbers of infiltrating T lymphocytes. To better understand the nature of the T cell response in this disease, we analyzed TCR expression in the brain lesions using PCR for quantitative assessment of TCRBV gene transcripts, together with size and sequence analysis of the third complementarity-determining region (CDR3) of the dominant TCR rearrangements. Restricted (oligoclonal) BV family usage was not observed, as all of the 22 BV PCR products were usually detected at levels exceeding the background. However, significant individual biases in the frequencies of different TCR families was evident. The distinct pattern of BV expression by infiltrating lymphocytes detected in the original PCR screening suggested a specific immune response. The primary structure of the rearranged CDR3 sequences for the BV family expressed at highest level in each sample was studied by size and sequence analysis. The data showed that predominant TCR BV families expressed in diseased brain tissue displayed limited size heterogeneity and extensive repetition of in-frame CDR3 nucleotide motifs. These findings demonstrate that the local immune response in Rasmussen's syndrome includes restricted T cell populations that have likely expanded from a few precursor T cells responding to discrete antigenic epitopes.

PMID: 9013988 [PubMed - indexed for MEDLINE]

1: J Immunol 2000 Aug 15;165(4):2020-7

Antigen triggering selectively increases TCRBV gene transcription.

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When the TCR binds Ag it is phosphorylated, internalized, and degraded. We wished to examine whether this process was accompanied by a specific concomitant increase in TCR mRNA levels. To do this, PBMC and a T cell clone were cultured with a series of superantigens and an alloantigen. Only T cells specifically responding to an antigenic stimulus had increased levels of TCR beta-chain variable (TCRBV)-specific mRNA. This response was apparent after 48 h, peaked around 72 h, and was still elevated after 7 days. Increased gene transcription appeared to be driven solely by Ag as specific Ag depletion prevented culture supernatants transferring this effect. The level of TCRBV mRNA elevation was not influenced by the stimulating Ag, but appeared dependent on the gene encoding the stimulated TCR. Reporter gene assays, using cloned TCRBV gene promoters, confirmed both that TCR gene transcription rises after stimulation and that basal and stimulated levels of TCR transcription vary between different TCRBV genes. These data conclusively demonstrate that there is no direct relationship between TCRBV mRNA and T cell number, and that future repertoire studies must take both factors into account.

PMID: 10925285 [PubMed - indexed for MEDLINE]

1: Eur J Oral Sci 1997 Oct;105(5 Pt 1):397-404

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Expression of T-cell receptor Vbeta2, 6 and 8 gene families in chronic adult periodontal disease.

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Substantial evidence exists to suggest a role for T-cells in periodontal disease. As yet, however, the T-cell receptors remain to be characterised at the molecular level. The expression and the nucleotide sequence of genes from the T-cell receptor beta variable (TCRBV) gene families 2, 6 and 8 were analyzed in periodontal tissue from 24 patients with chronic adult periodontal disease (CAPD) and peripheral blood lymphocytes (PBL) of 16 of these patients. A restriction in the expression of these TCRBV gene families was detected in periodontal tissue from 14/24 patients with CAPD, and the pattern of gene expression was often different between individual patients; however there was no restriction in TCRBV gene expression in matched PBL samples from 8 of these 14 patients. Quantitative RT PCR analysis of samples from 5 CAPD patients who expressed all 3 TCRBV gene families in their periodontal tissues did not reveal any significant differences in the levels of gene expression in periodontal tissue and PBL. In contrast to the findings with some CAPD patients, genes from all 3 TCRBV families were always expressed in periodontal tissue and PBL from disease-free control subjects. PCR products from both the PBL and periodontal tissue of CAPD patients were cloned and sequenced; analysis of the nucleotide sequence revealed diversity with respect to the expression of TCRB joining (TCRBJ) and TCRB diversity (TCRBD) genes and the sequence of the junctional region in all samples analysed. In conclusion, in CAPD, the pattern of TCRBV gene expression in periodontal tissue is often but not always different from that in PBL and healthy periodontal tissue, which may indicate, in some cases, a local influence on particular T-cell subsets which is relevant to the pathogenesis of periodontal disease. However, the expressed TCRB genes are heterogeneous at the nucleotide level, emphasising the underlying complexity at the molecular level in the local T-cell response in CAPD.

1: Clin Exp Immunol 2000 Apr;120(1):154-61

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Selective expansion of T cells in gingival lesions of patients with chronic inflammatory periodontal disease.

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Chronic inflammatory periodontal diseases are characterized by a cellular infiltrate and are similar in many respects to other chronic inflammatory diseases. While periodontopathic bacteria have been recognized as the principal causative agent and the immune response to these bacteria is thought to be responsible for the tissue destruction, the full aetiological spectrum is still incompletely understood. In addition to many cell types such as polymorphonuclear leucocytes and macrophages, T cells have been implicated in pathogenesis and are considered to have regulatory roles in progression of the disease. Based on our recent studies demonstrating biased expression of several Vbeta families in periodontitis tissues, the aim of this study was to characterize further the T cells relevant to the disease process by reverse transcription-polymerase chain reaction-single-strand conformation polymorphism (RT-PCR-SSCP) and subsequent nucleotide sequence analysis of complementarity-determining region 3 (CDR3) of the TCR beta-chain. In spite of the likely involvement of numerous bacteria, the present study has clearly shown the oligoclonality of infiltrating T cells in periodontitis lesions in contrast to low clonality of peripheral blood T cells as evidenced by the appearance of distinct bands in gingival tissue samples and smear pattern of peripheral blood on SSCP gels. These were confirmed by the DNA sequencing of the CDR3 of Vbeta16 of selected samples. The analysis of deduced amino acid sequences demonstrated amino acid motifs in the CDR3 region of the periodontitis lesion-derived sequences from each patient. The results indicate that gingival tissue-infiltrating T cells recognizing a limited number of antigens or epitopes are involved in the disease process.

PMID: 10759777 [PubMed - indexed for MEDLINE]